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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,874	12/11/2001	Edward B. Goldberg	NANF.P-007	4607

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EXAMINER	
KAUSHAL, SUMESH	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 12/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,874	GOLDBERG, EDWARD B.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7-21 and 24-48* is/are pending in the application.

4a) Of the above claim(s) *25-45 and 48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-21 and 24* is/are rejected.

7)☒ Claim(s) *46 and 47* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-4, 7-21 and 24-48 are pending.

Claims 1-4, 7-24 and 46-47 and are examined in this office action.

*Applicants are required to follow Amendment Practice under revised 37 CFR §1.121 (http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/revamdtprac.htm). The fax phone numbers for the organization where this application or proceeding is assigned is **703-872-9306**.*

Election/Restrictions

Applicant's election with traverse of Group I claims 1-4, 7-24 and 46-47 in Paper No. 09/05/03 is acknowledged. The traversal is on the ground(s) that inventions related to proteins and nucleic acid sequences, therefore does not lack unity. This is not found persuasive because MPEP clearly states that an international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories: 1) A product and a process specially adapted for the manufacture of said product; or 2) A product and a process of use of said product; or 3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or the said product; or 4) A process and an apparatus or means specifically designed for carrying out the said process; or 5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process (MPEP 37 CFR 1.475 (b)). In instant case the special technical feature of Group-I is T4 gp35 protein. The special technical feature of Group-II

is DNA and DNA-constructs encoding the T4 gp35 protein. Proteins and nucleic acid are structurally and functionally different compounds with different uses. For example proteins can be used to study protein-receptor interactions. The DNA can be used nucleic acid probe for hybridization procedures. Furthermore, the proteins can be isolated from host cells endogenously expressing the polypeptide, rather than by recombinant means. Thus, these inventions are technically distinct products of separate uses.

The requirement is still deemed proper and is therefore made FINAL.

Claims 25-45 and 48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 09/05/03.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Goldberg (WO 96/11947, 1996).

Claims 1 and 2 are drawn to a purified composition comprising a gp35 or bacteriopahge T4 gp35 protein not contained in a gel. Goldberg teaches isolated polypeptide consisting essentially of bacteriphage T4 p35 protein (see page 48, page 55, line 15-36; page 60 lines 1-4). The cited art teaches the isolation of recombinant gp35 protein using standard chromatography techniques including gel filtration and affinity chromatography (page 20). Thus given the broadest reasonable interpretation the cited art clearly anticipate the invention as claimed, since the gp35 as claimed is not limited to a particular amino acid sequence.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 7-21 and 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The scope of invention as claimed encompasses a composition comprising any gp35 protein or bacteriophage T4 gp35 protein. The scope of invention as claimed further encompasses any variant of amino acid sequences encoding SEQ ID NO:2 with one or more conservative substitution relative to the amino acid sequences found in

SEQ ID NO:2. The scope of invention as claimed further encompasses variants of SEQ ID NO:2 from amino acid numbers 1-17, 1-56, 1-78, 1-93, 8-17, 57-93, 57-64, 66-79 and 81-93 with one or more conservative substitutions relative to the amino acid sequence of SEQ ID NO:2. The scope of invention as claimed further encompasses variants of a protein encoded by SEQ ID NO: 2 that binds to the p34 protein of bacteriophage T4 or to an antibody directed against any gp35 protein (*not limited to gp35 of bacteriophage T4)* or a ligand. In addition the variants as claimed further encompasses a molecule comprising amino acid sequences having at least 30 or 60% identity to amino acid numbers 57-93 in SEQ ID NO:2 over 36 amino acid sequences.

At best the specification only disclose that the amino acid sequence of SEQ ID NO:2 which encodes the bacteriphage T4 gp35 protein. The specification disclosed that the phage T4 gp35 is located between genes gp34 and gp36. The specification further disclosed that two open reading frames ORF34.1 and ORF35 actually connect to form a single ORF35, which encodes a protein of about 40,000 Daltons. The specification further disclosed cloning of ORF35 by PCR of phage DNA between 5'-ATG start codon of ORF34.1 and 3'TAA stop codon of ORF35, which yield a sequence of approximately 1,120 nucleotides in length. However the specification as filed fails to define any variant of gp35 (other than SEQ ID NO:2) which has gp35 like activity explicitly or implicitly as putatively claimed herein.

Applicant is referred to the guidelines for ***Written Description Requirement*** published January 5, 2001 in the Federal Register, Vol.66, No.4, pp.1099-1110 (see http://www.uspto.gov). The disclosure of a single species is rarely, if ever, sufficient to

describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see In re Shokal 113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000). In the instant case the specification only disclose that the amino acid sequence of SEQ ID NO:2 which encodes the bacteriphage T4 gp35 protein. The specification fails to disclose any other variant of SEQ ID NO:2 as putatively claimed herein. The possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).* In claims to genetic material, generic statement such as "vertebrate insulin cDNA" or mammalian insulin cDNA," without more, is not adequate written description of claimed genus, since it does not distinguish genus from others except by function, and does not specifically define any of genes that fall within its definition, or describe structural features commonly possessed by members of genus that distinguish them from others; accordingly, naming type of material generally known to exist, in absence of knowledge as to what that material consists of, is not description of that material (*Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406).*

In the instant case the gp35 or SEQ ID NO:2 variants (as claimed) has been defined only by a statement of function that broadly encompasses a bacteriphage T4 gp35 protein like activity, an affinity for any gp35 antibody or an affinity for bacteriophage T4 gp34 protein, which conveyed no distinguishing information about the identity of the claimed gp35 protein variants, such as its relevant structural or physical characteristics. Furthermore the variation as claimed also encompasses unknown conserved motifs, since the specification as filed fails to define what are the conserved amino acid sequences which one skill in the art would considered germane for any bacteriphage T4 gp35 protein activity.

Furthermore 40-70% variation (30-60% identity, see claim 20-21) as claimed would certainly affect proper folding and biological activity if amino acids that are critical for such functions are substituted, since the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. Furthermore, mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues (see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994). Rudinger (in Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976). According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a

description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim.

Claims 1-4, 7-21 and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for bacteriphage T4 gp35 protein encoded by the amino acid sequences of SEQ ID NO:2, does not reasonably provide enablement for any gp35 protein any bactriophage T4 gp35 protein or variants of SEQ ID NO:2 (as claimed). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Nature of Invention:

The instant invention relates to isolated bacteriphage T4 gp35 protein.

Breadth of Claims and Guidance Provided in the Specification:

The scope of invention as claimed encompasses a composition comprising any gp35 protein or bacteriophage T4 gp35 protein. The scope of invention as claimed further encompasses any variant of amino acid sequences encoding SEQ ID NO:2 with one or more conservative substitution relative to the amino acid sequences found in SEQ ID NO:2. The scope of invention as claimed further encompasses variants of SEQ ID NO:2 from amino acid numbers 1-17, 1-56, 1-78, 1-93, 8-17, 57-93, 57-64, 66-79 and 81-93 with one or more conservative substitutions relative to the amino acid sequence of SEQ ID NO:2. The scope of invention as claimed further encompasses variants of a protein encoded by SEQ ID NO: 2 that binds to the p34 protein of bacteriophage T4 or to an antibody directed against any gp35 protein (*not limited to gp35 of bacteriophage*

T4) or a ligand. In addition the variants as claimed further encompasses a molecule comprising amino acid sequences having at least 30 or 60% identity to amino acid numbers 57-93 in SEQ ID NO:2 over 36 amino acid sequences.

At best the specification only disclose that the amino acid sequence of SEQ ID NO:2 which encodes the bacteriphage T4 gp35 protein. The specification disclosed that the phage T4 gp35 is located between genes gp34 and gp36. The specification further disclosed that two open reading frames ORF34.1 and ORF35 actually connect to form a single ORF35, which encodes a protein of about 40,000 Daltons. The specification further disclosed cloning of ORF35 by PCR of phage DNA between 5'-ATG start codon of ORF34.1 and 3'TAA stop codon of ORF35, which yield a sequence of approximately 1,120 nucleotides in length. However the specification as filed fails to define any variant of gp35 (other than SEQ ID NO:2) which has gp35 like activity explicitly or implicitly as putatively claimed herein.

State of Art and Predictability

The bacteriophage T4 is one of the archetypical members of the family Myoviridae or T-even phage. These viruses are characterized by a large, elongated icosohedral head; a contractile tail, and tail fibers. The tail fiber proteins have an unusual quaternary structure of long, thin and rigid rods. Their function is to transduce chemical recognition of the E. coli host into a mechanical force on the phage base plate, essentially acting as a set of cooperative levers. This mechanical stress triggers a series of protein conformational changes that lead to entry of the phage DNA into the cell. The three main tail fiber proteins, P34, P36 and P37, are thought to be principally composed of dimeric anti parallel-sheets. Gp35, which forms the angle in the tail fiber,

probably has a more complex structure. The joints between the homodimeric segments are also likely to have a more complex structure but there is no evidence that the central rod regions have any tertiary structure at all. The extended anti parallel -sheet secondary structure supports the rigid rod quaternary structure. (Hyman et al, PNAS 99(13): 8488-8493, 2002).

The instant application claims variants of the bacteriophage T4 gp35 protein, and provides no distinguishing information about the identity of the claimed variants, such as its relevant structural or physical characteristics. It is general knowledge in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. The variants as claimed are mere hypothetical possibilities because no biological functions have been established. The mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues. Therefore, applicant has not presented enablement commensurate in scope with the claims. see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994). Rudinger (in Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976). Therefore it would require an undue amount of experimentation to

make and test the all-possible variations for bateriopahge T4 gp35 protein, wherein each variant made has been defined by both structural and functional limitations.

Under the law, the disclosure "shall inform how to use, NOT how to find out how to use for themselves." See In re Gardner 475 F.2d 1389, 177 USPQ 396 (CCPA 1973). The bacteriphage T4 gp35 protein which forms the angle in the tail fiber is known to have a complex structure and without sufficient guidance to make a specific mutation in the disclosed amino acid sequences the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

Claim Objections

Claims 46-47 are objected to because of the following informalities: Instant claims depends upon claims 44 and 45, which encompasses the non-elected invention of group II. Appropriate correction is required.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 703-305-6838 (**571-272-0769**). The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel Ph.D. can be reached on 703-305-1998 (**571-272-0781**). The fax phone numbers for the organization where this application or proceeding is assigned is **703-872-9306**. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

S. Kaushal
Patent examiner

JEFFREY FREDMAN
PRIMARY EXAMINER